REMARKS

Claims 64-67, 71, 72, 76-78 and 80-113 are now pending. By this Amendment, claims 70, 73-75 and 79 are canceled; claims 64-66, 71-72 and 76-78 are amended; and claims 80-113 are added.

Applicants thank Examiner Hutson for the courtesies extended during the November 4, 2004 personal interview. Applicants' separate record of the substance of the interview is incorporated into the following remarks.

The specification is objected to based on the sentence added to the paragraph beginning at page 54, line 14. This sentence is deleted herein. Therefore, the objection should be withdrawn.

Claims 76-78 are objected to for being duplicates of claims 73-75. Although Applicants disagree with this objection, claims 73-75 have been canceled herein, rendering the objection moot.

Claims 64-67 and 70-79 are rejected under 35 U.S.C. §112, first paragraph, for allegedly not being enabled by the present specification. Applicants respectfully traverse the rejection.

An analysis of whether a particular claim is supported by the disclosure in an application requires a determination of whether the disclosure, when filed, contained sufficient information regarding the subject matter of the claims so as to enable one skilled in the pertinent art to make and use the claimed invention without undue experimentation. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). The fact that experimentation may be complex does not necessarily make it undue if the art typically engages in such experimentation. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. In re Angstadt, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976). It is respectfully submitted that based on

this standard, the present specification enables the subject matter of claims 64-67 and 70-79, as well as new claims 80-106.

Claim 64 is directed to isolated heparanase protein having heparanase catalytic activity or being cleavable so as to acquire heparanase catalytic activity, the protein consisting essentially of a polypeptide at least 70% homologous to SEQ ID NO: 10 or to a portion thereof. It is respectfully submitted that, at the time of the present invention, one of ordinary skill in the art would have been able to make and use the proteins of claim 64 without undue experimentation. Specifically, one of ordinary skill in the art would have been able to make and use the polypeptide of SEQ ID NO: 10. In addition, one of ordinary skill in the art would have been able to modify the polypeptide of SEQ ID NO: 10 in order to form other proteins within the scope of claim 64 having heparanase catalytic activity or being cleavable so as to acquire heparanase catalytic activity.

In particular, one of ordinary skill in the art would have been able, by routine experimentation, to synthesize proteins having the claimed level of homology with SEQ ID NO: 10, and to test these proteins (optionally after they have been cleaved) for heparanase catalytic activity. In addition, the sequence comparisons between human, mouse and rat heparanase presented in Figure 17 provides significant guidance as to modifications that can be made to the protein while retaining its heparanase catalytic activity. Furthermore, one of ordinary skill in the art is well aware of the characteristics of the various amino acids and the types of amino acid substitutions that are more likely to maintain a functional protein. Thus, given the high level of skill in the art, it is respectfully submitted that experimentation necessary to practice the full scope of claim 64 would not have been undue. In contrast, this type of experimentation would have been considered routine in the art.

Attached hereto is a Declaration of one of skill in the art, Dr. Iris Pecker, supporting the enablement position described herein. Further evidence supporting enablement of the

current claims was presented in the August 12, 2003 Declaration of Iris Pecker, which was filed in the above-identified patent application on April 19, 2004.

The other independent claims all recite a polypeptide at least 70% homologous to a specified sequence and that the heparanase protein has heparanase catalytic activity or is cleavable so as to acquire heparanase catalytic activity. In addition, many of the claims recite even greater degrees of percent homology, specifically, at least 80% homology, at least 90% homology or at least 95% homology. As discussed above, the specification clearly enables making and using a polypeptide having SEQ ID NO: 10, as well as modifying such a polypeptide in order to make and use heparanase proteins having at least 70% homology with SEQ ID NO: 10 or a portion thereof. In addition, the recitations in dependent claims of at least 80% homology, at least 90% homology and at least 95% homology further narrow the claim scope and are thus even more clearly enabled by the present specification.

The specification clearly enables claims 64-67, 71, 72 and 76-78, as well as new claims 80-113. Therefore, the rejection under 35 U.S.C. §112, first paragraph, should be reconsidered and withdrawn.

Claims 64-67 and 70-79 are rejected under 35 U.S.C. §102 over Fuks et al. Applicants respectfully traverse the rejection.

Claims 64 and 71 both recite isolated heparanase protein. As discussed in the Declaration of Dr. Pecker attached hereto, the composition described in Fuks contains a mixture of proteins and would not be considered isolated heparanase protein to one of ordinary skill in the art. Further support for this position is set forth in the June 12, 2003 Declaration of Israel Vlodavsky, which was filed in the above-identified patent application on April 19, 2004. In this Declaration, Dr. Vlodavsky, who is one of the inventors of Fuks, specifically acknowledges that the antibodies raised in Fuks in an attempt to prepare anti-heparanase antibodies were actually anti-PAI-1 antibodies. Thus, it is clear that the

composition described in Fuks contains a significant amount of PAI-1 relative to the amount of heparanase such that the composition would not be considered "isolated heparanase protein," as recited in claims 64 and 71.

Claim 76 and new claim 107 are directed to recombinant heparanase protein that has been purified close to homogeneity. As discussed in the paragraph above and in the Declaration of Dr. Pecker attached hereto, the composition described in Fuks contains a mixture of proteins. This mixture of proteins would not be considered by one of ordinary skill in the art to be heparanase protein "purified close to homogeneity," as recited in claims 76 and 107.

Claim 66 and new claim 97 are directed to a preparation comprising a protein component, the protein component consisting essentially of heparanase protein. Fuks does not teach a preparation in which the protein component consists essentially of heparanase protein. Instead, the composition obtained in Fuks contains a mixture of proteins. In particular, this composition contains a significant amount of PAI-1. In fact, it contains so much PAI-1 that the antibodies raised from the composition were anti-PAI-1 antibodies rather than anti-heparanase antibodies. See the Declaration attached hereto, the June 9, 2003 Declaration of Iris Pecker and the June 12, 2003 Declaration of Israel Vlodavsky, a co-inventor of Fuks. Thus, the protein component of the composition of Fuks does not consist essentially of heparanase protein. Similarly, Fuks does not teach the pharmaceutical compositions of claims 65, 72, 78 and new claim 112.

Fuks does not teach each and every feature of the present claims. Therefore, the rejection over Fuks should be reconsidered and withdrawn.

In view of the foregoing, it is respectfully submitted that this application is in condition for allowance. Favorable reconsideration and prompt allowance of claims 64-67, 71, 72, 76-78 and 80-113 are earnestly solicited.

Should the Examiner believe that anything further would be desirable in order to place this application in even better condition for allowance, the Examiner is invited to contact the undersigned at the telephone number set forth below.

Respectfully submitted,

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WPB:MLM/jam

Attachment:
132 Declaration

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